

09/600,786

=> d his; d l33 tot ibib abs hitstr

(FILE 'HOME' ENTERED AT 11:14:58 ON 30 SEP 2005)

FILE 'REGISTRY' ENTERED AT 11:15:13 ON 30 SEP 2005

L1 SCREEN 964 AND 1006 AND 1015  
L2 STRUCTURE UPLOADED  
L3 QUE L2 AND L1  
L4 0 S L3 FUL  
L5 SCREEN 963 AND 1006 AND 1015  
L6 STRUCTURE UPLOADED  
L7 QUE L6 AND L5  
L8 0 S L7 FUL  
L9 SCREEN 963 AND 970 AND 1006 AND 1015  
L10 STRUCTURE UPLOADED  
L11 QUE L10 AND L9  
L12 0 S L11 FUL  
L13 SCREEN 963 AND 1006 AND 1015  
L14 STRUCTURE UPLOADED  
L15 QUE L14 AND L13  
L16 0 S L15 FUL  
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L18 STRUCTURE UPLOADED  
L19 QUE L18 AND L17  
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L25 SCREEN 963 AND 1006 AND 1015  
L26 STRUCTURE UPLOADED  
L27 QUE L26 AND L25  
L28 28 S L27 FUL  
L29 SCREEN 963 AND 1006 AND 1015  
L30 STRUCTURE UPLOADED  
L31 QUE L30 AND L29  
L32 0 S L26 NOT L30

L33 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:78252 CAPLUS

DOCUMENT NUMBER: 142:176603

TITLE: Preparation of inhibitors of the anandamide transporter

INVENTOR(S): Makriyannis, Alexandros; Goutopoulos, Andreas; Li, Chen

PATENT ASSIGNEE(S): University of Connecticut, USA

SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 701,989.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005020679	A1	20050127	US 2004-899191	20040726
WO 9964389	A1	19991216	WO 1999-US12900	19990609
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.:

US 1998-88568P

P 19980609

WO 1999-US12900

W 19990609

US 2001-701989

B2 20010129

OTHER SOURCE(S): MARPAT 142:176603

AB Disclosed are compds., XYZ [X = fatty acid residue, aliphatic hydrocarbon, alkyl-substituted biphenyl; Y = NHC(:O), NH, NHC(:O)NH, NHC(:O)O, OC(:O)NH, C(:O)C(:O)NH, NHC(:O)C(:O), OC(:O)O, C(:O)NH, OC(:O), O, S, H (wherein X and Z may be connected to Y at either of the Y portion connecting atoms); Z = H, (un)substituted aryl, (un)substituted alkyl, alkylaryl, haloalkylaryl, (un)substituted cyclic glycerols, COCF<sub>3</sub>, C(:O)-alc., (CH<sub>2</sub>)<sub>m</sub>(CMe<sub>2</sub>)<sub>p</sub>(CH<sub>2</sub>)<sub>n</sub>T<sub>2</sub>T<sub>3</sub>, (CH<sub>2</sub>)<sub>m</sub>(CHMe)<sub>q</sub>(CH<sub>2</sub>)<sub>n</sub>T<sub>2</sub>T<sub>3</sub>; m, n = 0 -6; p, q = 0, 1; T<sub>2</sub> = optional aryl, mono-, bi-, tricyclic, heterocyclic, heterobicyclic, heterotricyclic, heteroarom., linear or cyclic 1- or 2-glycerol, alkyl, alkenyl, alkynyl; T<sub>3</sub> = H, OH, SH, halogen, C(halogen)<sub>3</sub>, CH(Halogen)<sub>2</sub>, O-alkyl, N<sub>3</sub>, CN, NCS, NH<sub>2</sub>, alkylamino, dialkylamino; with the proviso that Z ≠ C<sub>6</sub>H<sub>4</sub>OH-4 if XY = AA-CO-NH; AA = (CH<sub>2</sub>)<sub>3</sub>(CH:CHCH<sub>2</sub>)<sub>4</sub>Bu-(Z,Z,Z,Z)] and their physiol. acceptable salts, that are anandamide transport inhibitors and their pharmacol. use. Thus, AA-CH<sub>2</sub>NHC(:O)OCH<sub>2</sub>CHMeOH-(S) was prepared from Me arachidonate via reduction

with

LiAlH<sub>4</sub> in Et<sub>2</sub>O, tosylation, azidation, with LiAlH<sub>4</sub> in Et<sub>2</sub>O/THF, carbonylation with carbonyl diimidazole, reaction with HOCH<sub>2</sub>CHMeOH-(S) and desilylation with Bu<sub>4</sub>NF in THF. Fatty acid derivs., e.g., AA-CH<sub>2</sub>OC(O)NHR, were tested for their inhibitory activity against anandamide transporter [IC<sub>50</sub> = 7.1 μM {R = CHMeCH<sub>2</sub>OH-(R)}; IC<sub>50</sub> = 6.4 μM {R = CHMeCH<sub>2</sub>OH-(S)}; IC<sub>50</sub> = 1.5 μM {R = CH<sub>2</sub>CHMeOH-(R)}; IC<sub>50</sub> = 0.4 μM {R = CH<sub>2</sub>CHMeOH-(S)}; IC<sub>50</sub> = 21.9 μM {R = CHMe<sub>2</sub>}; IC<sub>50</sub> = 15.5 μM {R = cyclopropyl}; IC<sub>50</sub> = 15.5 μM {R = cyclobutyl}; IC<sub>50</sub> = 33.0 μM {R = cyclohexyl}; IC<sub>50</sub> = 6.6 μM {R = C<sub>6</sub>H<sub>4</sub>OH-4}; IC<sub>50</sub> = 16.1 μM {R = 3-pyridyl}].

IT 251908-91-5 251908-92-6, AM1172

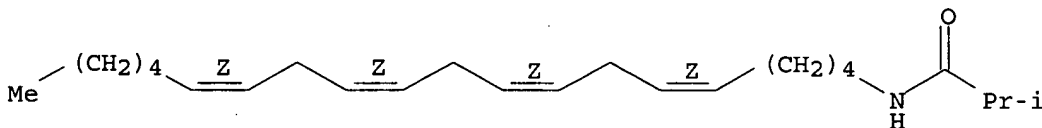
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition by, of anandamide transporter; preparation of inhibitors of the anandamide transporter)

RN 251908-91-5 CAPLUS

CN Propanamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-2-methyl- (9CI)  
(CA INDEX NAME)

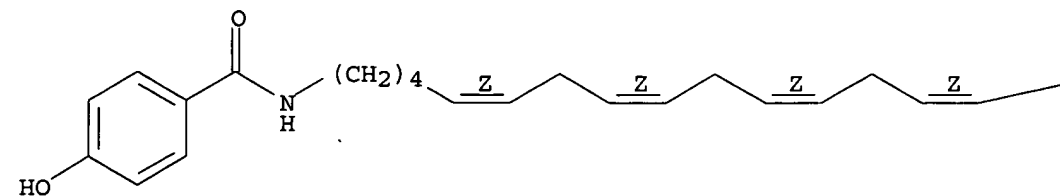
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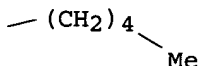


RN 251908-92-6 CAPLUS

CN Benzamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-4-hydroxy- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.





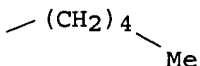
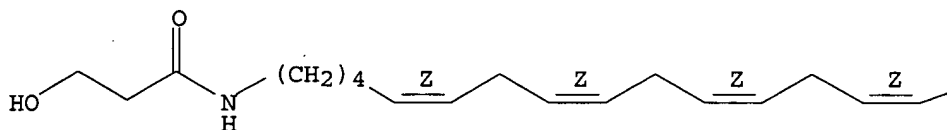
IT 220556-77-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of inhibitors of the anandamide transporter)

RN 220556-77-4 CAPLUS

CN Propanamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-3-hydroxy- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



L33 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:516740 CAPLUS

DOCUMENT NUMBER: 141:117582

TITLE: Anandamide transport is independent of fatty-acid  
amide hydrolase activity and is blocked by the  
hydrolysis-resistant inhibitor AM1172

AUTHOR(S): Fegley, D.; Kathuria, S.; Mercier, R.; Li, C.;  
Goutopoulos, A.; Makriyannis, A.; Piomelli, D.

CORPORATE SOURCE: Department of Pharmacology, University of California,  
Irvine, CA, 92697-4625, USA

SOURCE: Proceedings of the National Academy of Sciences of the  
United States of America (2004), 101(23), 8756-8761  
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The endogenous cannabinoid anandamide is removed from the synaptic space by a high-affinity transport system present in neurons and astrocytes, which is inhibited by N-(4-hydroxyphenyl)-arachidonamide (AM 404). After internalization, anandamide is hydrolyzed by fatty-acid amide hydrolase (FAAH), an intracellular membrane-bound enzyme that also cleaves AM 404. Based on kinetic evidence, it has recently been suggested that anandamide internalization may be mediated by passive diffusion driven by FAAH activity. To test this possibility, in the present study, we have investigated anandamide internalization in wild-type and FAAH-deficient (FAAH-/-) mice. Cortical neurons from either mouse strain internalized

[3H]anandamide through a similar mechanism, i.e., via a rapid temperature-sensitive and saturable process, which was blocked by AM 404. Moreover, systemic administration of AM 404 to either wild-type or FAAH-/- mice enhanced the hypothermic effects of exogenous anandamide, a response that was prevented by the CB1 cannabinoid antagonist rimonabant (SR 141716A). The results indicate that anandamide internalization in mouse brain neurons is independent of FAAH activity. In further support of this conclusion, the compound N-(5Z,8Z,11Z,14Z-eicosatetraenyl)-4-hydroxybenzamide (AM 1172) blocked [3H]anandamide internalization in rodent cortical neurons and human astrocytoma cells without acting as a FAAH substrate or inhibitor. AM 1172 may serve as a prototype for novel anandamide transport inhibitors with increased metabolic stability.

IT 251908-92-6, AM 1172

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

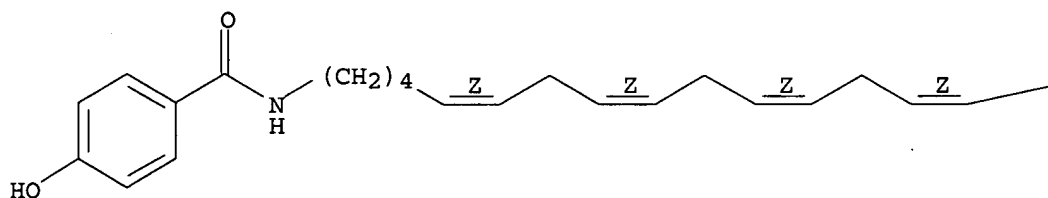
(anandamide transport is independent of fatty-acid amide hydrolase activity and is blocked by hydrolysis-resistant inhibitor AM 1172 in rodent cortical neurons and human astrocytoma cells)

RN 251908-92-6 CAPLUS

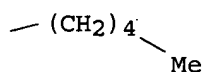
CN Benzamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-4-hydroxy- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:300461 CAPLUS

DOCUMENT NUMBER: 134:305335

TITLE: Retro-anandamides, high affinity and stability  
cannabinoid receptor ligands

INVENTOR(S): Makriyannis, Alexandros; Liu, Qian; Goutopoulos, Andreas

PATENT ASSIGNEE(S): University of Connecticut, USA

SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001028498 A2 20010426 WO 2000-US41248 20001018  
 WO 2001028498 A3 20010913  
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2387846 AA 20010426 CA 2000-2387846 20001018  
 AU 2001019692 A5 20010430 AU 2001-19692 20001018  
 EP 1226112 A2 20020731 EP 2000-982697 20001018  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL  
 JP 2003511478 T2 20030325 JP 2001-531094 20001018  
 ZA 2002003910 A 20040126 ZA 2002-3910 20020516  
 PRIORITY APPLN. INFO.: US 1999-160033P P 19991018  
 WO 2000-US41248 W 20001018

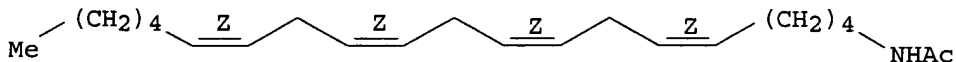
OTHER SOURCE(S): MARPAT 134:305335

AB Novel retro-anandamides are presented which have high affinities for the cannabinoid CB1 and/or CB2 receptor sites. Further, most of the analogs exhibit greater metabolic stability than arachidonylethanolamide. The improved receptor affinity and selectivity and/or greater metabolic stability make these analogs therapeutically useful as medications in individuals and animals for treatment of pain, glaucoma, epilepsy, nausea associated with chemotherapy, as well as suppression of the immune system, enhancement of appetite and in treatment of certain mental disorders.

IT 215818-35-2P 335372-49-1P 335372-50-4P  
 335372-51-5P 335372-52-6P 335372-53-7P  
 335372-55-9P 335372-56-0P 335372-58-2P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of retroanandamides, high affinity and stability cannabinoid receptor ligands)

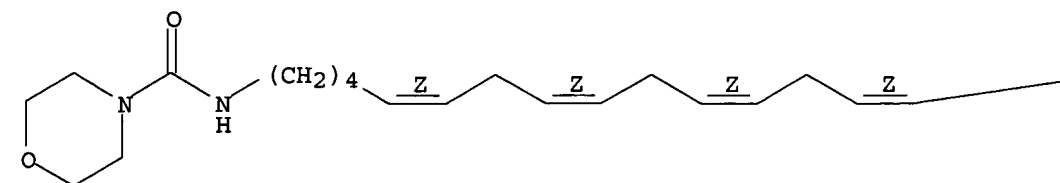
RN 215818-35-2 CAPLUS  
 CN Acetamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

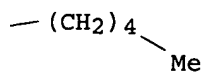


RN 335372-49-1 CAPLUS  
 CN 4-Morpholinecarboxamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



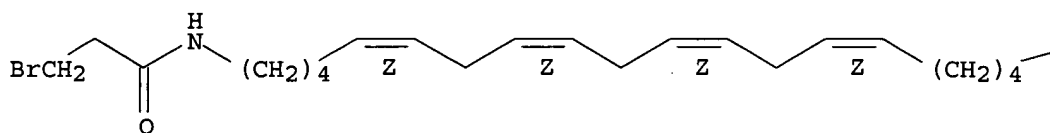
PAGE 1-B



RN 335372-50-4 CAPLUS  
 CN Propanamide, 3-bromo-N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A

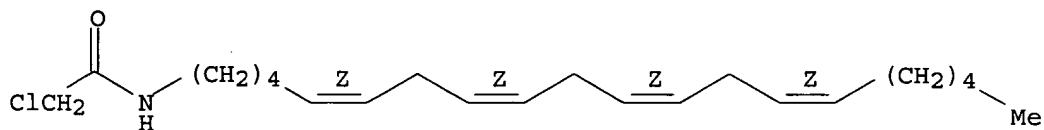


PAGE 1-B



RN 335372-51-5 CAPLUS  
 CN Acetamide, 2-chloro-N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI)  
 (CA INDEX NAME)

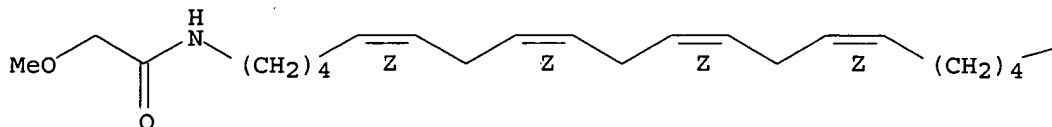
Double bond geometry as shown.



RN 335372-52-6 CAPLUS  
 CN Acetamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-2-methoxy- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



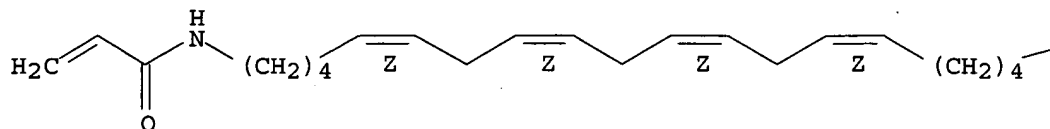
RN 335372-53-7 CAPLUS

09/600,786

CN 2-Propenamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

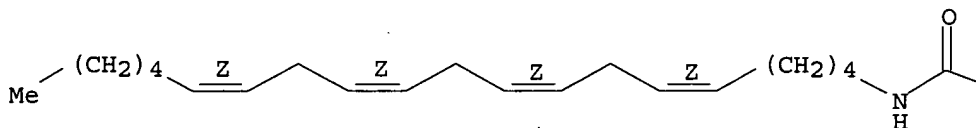
Me

RN 335372-55-9 CAPLUS

CN Acetamide, 2,2-dichloro-N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



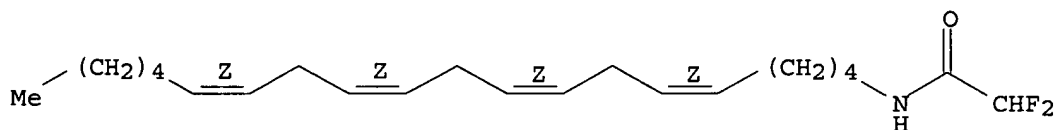
PAGE 1-B

CHCl<sub>2</sub>

RN 335372-56-0 CAPLUS

CN Acetamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-2,2-difluoro- (9CI) (CA INDEX NAME)

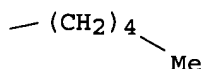
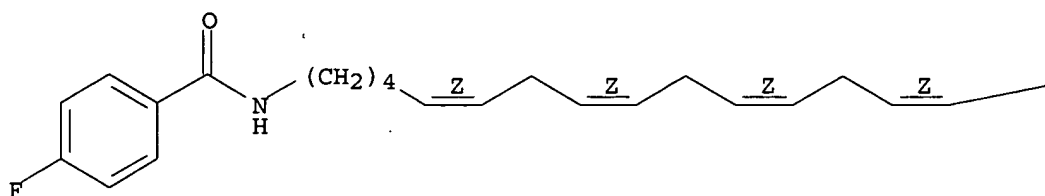
Double bond geometry as shown.



RN 335372-58-2 CAPLUS

CN Benzamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-4-fluoro- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L33 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2000:383939 CAPLUS  
 DOCUMENT NUMBER: 133:26865  
 TITLE: Cannabimimetic arachidonylethanolamide (anandamide) derivatives as useful medications, and preparation thereof  
 INVENTOR(S): Makriyannis, Alexandros; Khanolkar, Atmaram; Goutopoulos, Andreas  
 PATENT ASSIGNEE(S): USA  
 SOURCE: PCT Int. Appl., 28 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000032200	A1	20000608	WO 1999-US28136	19991124
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1049474	A1	20001108	EP 1999-961838	19991124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			US 1998-109615P	P 19981124
			WO 1999-US28136	W 19991124

OTHER SOURCE(S): MARPAT 133:26865

AB Analogs of arachidonylethanolamide (anandamide) are provided which have higher affinities for the cannabinoid CB1 and/or CB2 receptor sites. Further, most of the analogs exhibit greater metabolic stability than arachidonylethanolamide. The improved receptor affinity and selectivity and/or greater metabolic stability make these analogs therapeutically useful as medications for relief of pain caused by cancer and nausea caused by chemotherapy, as well as for peripheral pain. The compds. may also be useful as oral and topical contraceptives, in suppression of the

immune system, enhancement of appetite and in treatment of psychomotor disorders, multiple sclerosis and hypertension.

IT 273734-21-7P

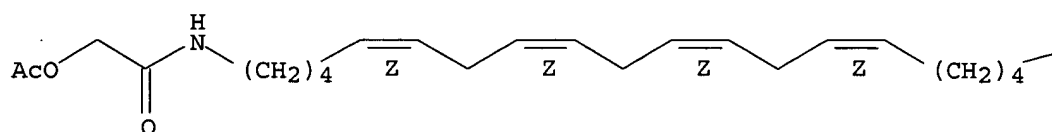
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(cannabimimetic arachidonylethanolamide derivative preparation for useful medication)

RN 273734-21-7 CAPLUS

CN Acetamide, 2-(acetyloxy)-N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

Me

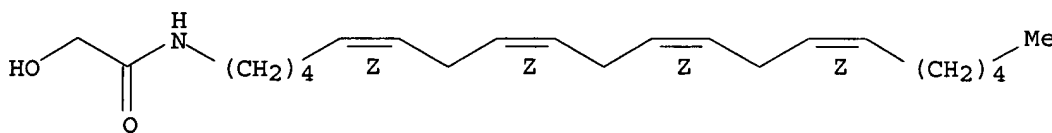
IT 273734-23-9

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(cannabimimetic arachidonylethanolamide derivative preparation for useful medication)

RN 273734-23-9 CAPLUS

CN Acetamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-2-hydroxy- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



IT 220556-77-4 220556-78-5 273734-10-4  
273734-11-5 273734-12-6 273734-13-7

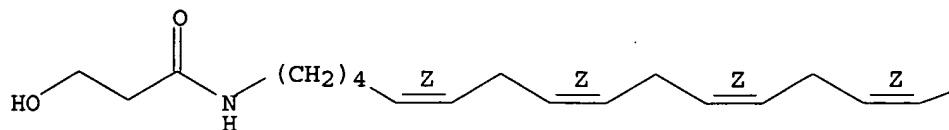
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cannabimimetic arachidonylethanolamide derivative preparation for useful medication)

RN 220556-77-4 CAPLUS

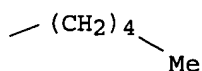
CN Propanamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-3-hydroxy- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

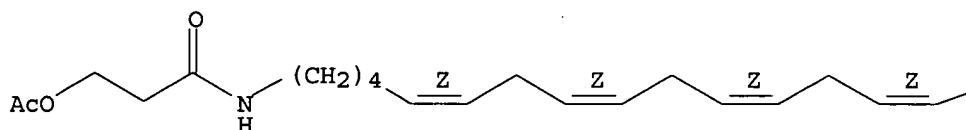


RN 220556-78-5 CAPLUS

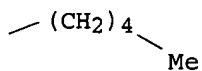
CN Propanamide, 3-(acetyloxy)-N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

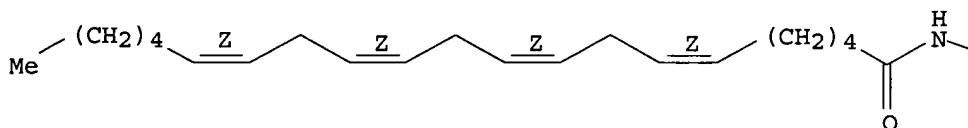


RN 273734-10-4 CAPLUS

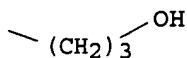
CN 6,9,12,15-Heneicosatetraenamide, N-(3-hydroxypropyl)-, (6Z,9Z,12Z,15Z)-  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



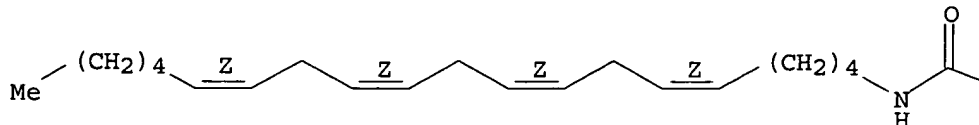
RN 273734-11-5 CAPLUS

09/600,786

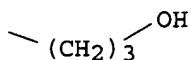
CN Butanamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-4-hydroxy- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



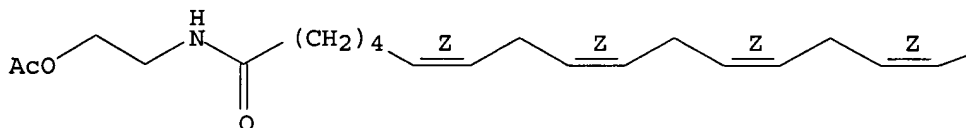
PAGE 1-B



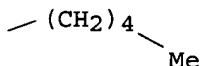
RN 273734-12-6 CAPLUS  
CN 6,9,12,15-Heneicosatetraenamide, N-[2-(acetyloxy)ethyl]-, (6Z,9Z,12Z,15Z)-  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



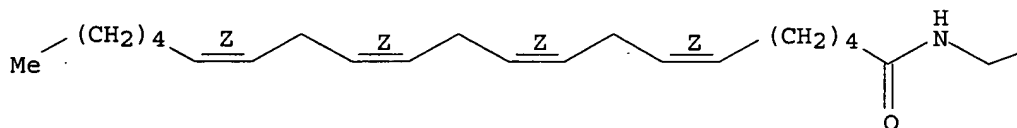
PAGE 1-B

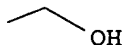


RN 273734-13-7 CAPLUS  
CN 6,9,12,15-Heneicosatetraenamide, N-(2-hydroxyethyl)-, (6Z,9Z,12Z,15Z)-  
(9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

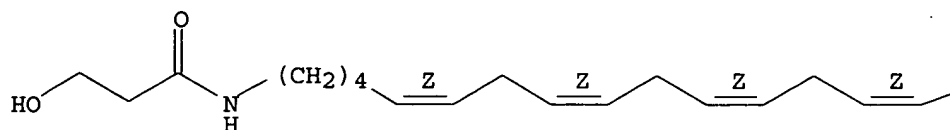
L33 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1999:795784 CAPLUS  
 DOCUMENT NUMBER: 132:22820  
 TITLE: Preparation of arachidonyl amine amides as inhibitors of the anandamide transporter and their use as analgesics  
 INVENTOR(S): Makriyannis, Alexandros; Lin, Sonyuan; Piomelli, Daniele; Goutopoulos, Andreas  
 PATENT ASSIGNEE(S): USA  
 SOURCE: PCT Int. Appl., 28 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964389	A1	19991216	WO 1999-US12900	19990609
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2337822	AA	19991216	CA 1999-2337822	19990609
EP 1084098	A1	20010321	EP 1999-930176	19990609
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002517479	T2	20020618	JP 2000-553399	19990609
US 2005020679	A1	20050127	US 2004-899191	20040726
PRIORITY APPLN. INFO.:			US 1998-88568P	P 19980609
			WO 1999-US12900	W 19990609
			US 2001-701989	B2 20010129

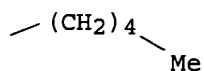
OTHER SOURCE(S): MARPAT 132:22820  
 AB Arachidonyl amine amides (e.g., arachidonyl amine 4-hydroxybenzoic acid amide; IC50 50 nM) were prepared and tested as competitive anandamide transport inhibitor,s and their use as analgesics (no data) is proposed.  
 IT 220556-77-4P 251908-91-5P 251908-92-6DP,  
 tritiated derivs. 251908-92-6P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of arachidonyl amine amides as inhibitors of the anandamide transporter and their use as analgesics)  
 RN 220556-77-4 CAPLUS  
 CN Propanamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-3-hydroxy- (9CI)  
 (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



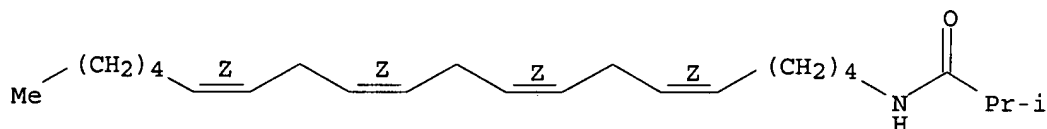
PAGE 1-B



RN 251908-91-5 CAPLUS

CN Propanamide, N- (5Z,8Z,11Z,14Z) -5,8,11,14-eicosatetraenyl-2-methyl- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.

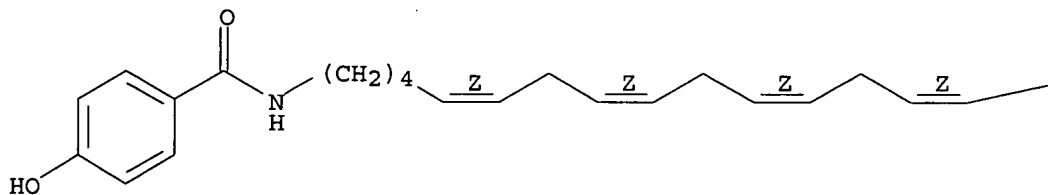


RN 251908-92-6 CAPLUS

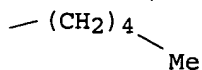
CN Benzamide, N- (5Z,8Z,11Z,14Z) -5,8,11,14-eicosatetraenyl-4-hydroxy- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



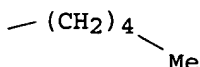
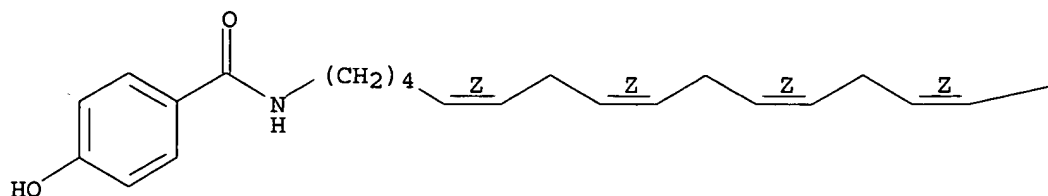
PAGE 1-B



RN 251908-92-6 CAPLUS

CN Benzamide, N- (5Z,8Z,11Z,14Z) -5,8,11,14-eicosatetraenyl-4-hydroxy- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:786633 CAPLUS

DOCUMENT NUMBER: 130:177116

TITLE: Novel Analogs of Arachidonylethanolamide (Anandamide): Affinities for the CB1 and CB2 Cannabinoid Receptors and Metabolic Stability

AUTHOR(S): Lin, Sonyuan; Khanolkar, Atmaram D.; Fan, Pusheng; Goutopoulos, Andreas; Qin, Ce; Papahadjis, Demetris; Makriyannis, Alexandros

CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Connecticut, Storrs, CT, 06269, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(27), 5353-5361

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 130:177116

AB Several analogs of the endogenous cannabinoid receptor ligand arachidonylethanolamide (anandamide) were synthesized and evaluated to study (a) the structural requirements for high-affinity binding to the CB1 and CB2 cannabinoid receptors and (b) their hydrolytic stability toward anandamide amidase. The series reported here was aimed at exploring structure-activity relationships (SAR) primarily with regard to stereoelectronic requirements of ethanolamido headgroup for interaction with the cannabinoid receptor active site. Receptor affinities, reported as  $K_i$  values, were obtained by a standard receptor binding assay using [ $^3$ H]CP-55,940 as the radioligand, while stability toward the amidase was evaluated by comparing the  $K_i$  of each analog in the presence and absence of phenylmethanesulfonyl fluoride (PMSF), a serine protease blocker and inhibitor of anandamide amidase. Introduction of a Me group in the 1'- and 2'-positions or substitution of the ethanolamido headgroup with a butylamido group gave analogs with vastly improved biochem. stability. This is accomplished in some cases with increased receptor affinity. Conversely, oxazolyl and methyloxazolyl headgroups led to low-affinity analogs. Substitution of the hydroxyl group with electroneg. substituents such as fluoro, chloro, allyl, and propargyl groups significantly increased receptor affinity but did not influence the biochem. stability. The 2'-chloro analog of anandamide was found to have the highest affinity for CB1. Addnl., reversing the positions of the carbonyl and NH in the

amido group produces retro-anandamides possessing considerably higher metabolic stability. Replacement of the arachidonyl tail with oleyl or linoleyl results in analogs with low affinities for both receptors. All of the analogs in this study showed high selectivity for the CB1 receptor over the peripheral CB2 receptor. The most potent analogs were tested for their ability to stimulate the binding of [35S]GTPyS to G-proteins and were shown to be potent cannabimimetic agonists. The results are discussed in terms of pharmacophoric features affecting receptor affinity and enzymic stability.

IT 220556-77-4P 220556-78-5P

RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

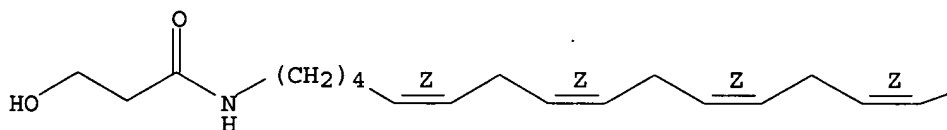
(preparation of novel analogs of arachidonylethanolamide (anandamide) and affinities for CB1 and CB2 cannabinoid receptors and metabolic stability toward anandamide amidase)

RN 220556-77-4 CAPLUS

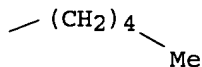
CN Propanamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl-3-hydroxy- (9CI)  
(CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

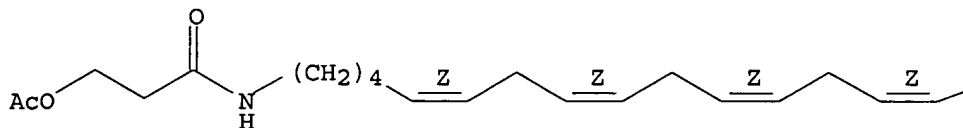


RN 220556-78-5 CAPLUS

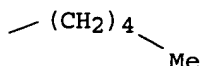
CN Propanamide, 3-(acetyloxy)-N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



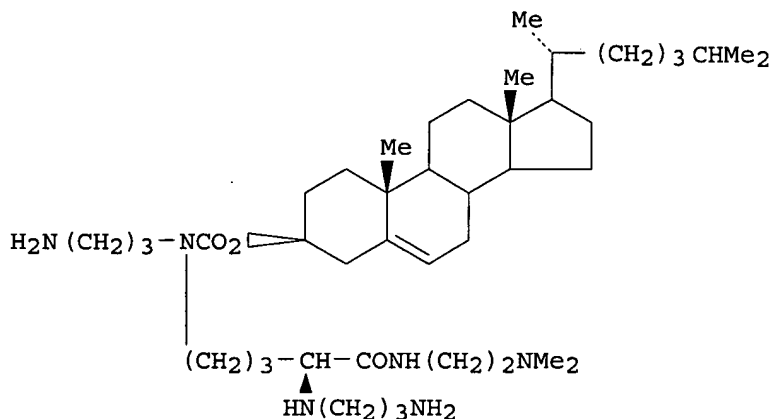
PAGE 1-B



RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1998:684856 CAPLUS  
 DOCUMENT NUMBER: 129:306524  
 TITLE: Cationic amphiphiles for intracellular delivery of therapeutic molecules  
 INVENTOR(S): Siegel, Craig S.; Lee, Edward R.; Harris, David J.  
 PATENT ASSIGNEE(S): Genzyme Corp., USA  
 SOURCE: PCT Int. Appl., 79 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9843994	A1	19981008	WO 1998-US6169	19980330
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5925628	A	19990720	US 1997-828234	19970331
AU 9867846	A1	19981022	AU 1998-67846	19980330
PRIORITY APPLN. INFO.:			US 1997-828234	A 19970331
			WO 1998-US6169	W 19980330
OTHER SOURCE(S):		MARPAT 129:306524		
GI				



AB Novel cationic amphiphiles are provided that facilitate transport of biol. active (therapeutic) mols. into cells. There are provided also therapeutic compns. prepared typically by contacting a dispersion of one or more cationic amphiphiles with the therapeutic mols. Therapeutic mols. that can be delivered into cells according to the practice of the invention include DNA, RNA, and polypeptides. Representative uses of the therapeutic compns. of the invention include providing gene therapy, and delivery of antisense polynucleotides or biol. active polypeptides to cells. With respect to therapeutic compns. for gene therapy, the DNA is provided typically in the form of a plasmid for complexing with the cationic amphiphile. An example amphiphile prepared was I. Other examples given were cell transfection assay, CAT assay, construction of vectors, and correction of Cl<sup>-</sup> transport defect in airway epithelial cells of a cystic fibrosis patient by cationic amphiphile-mediated gene transfer.

09/600,786

IT 214398-83-1

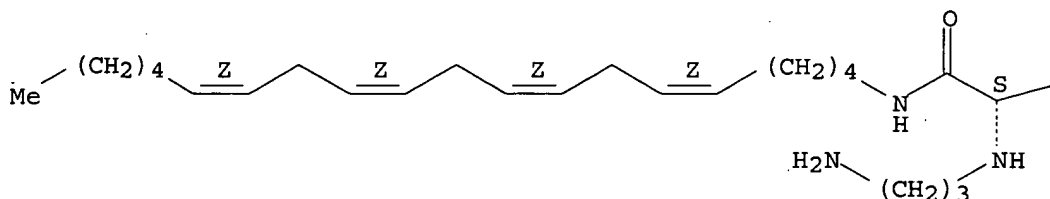
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cationic amphiphiles for intracellular delivery of therapeutic mols.)

RN 214398-83-1 CAPLUS

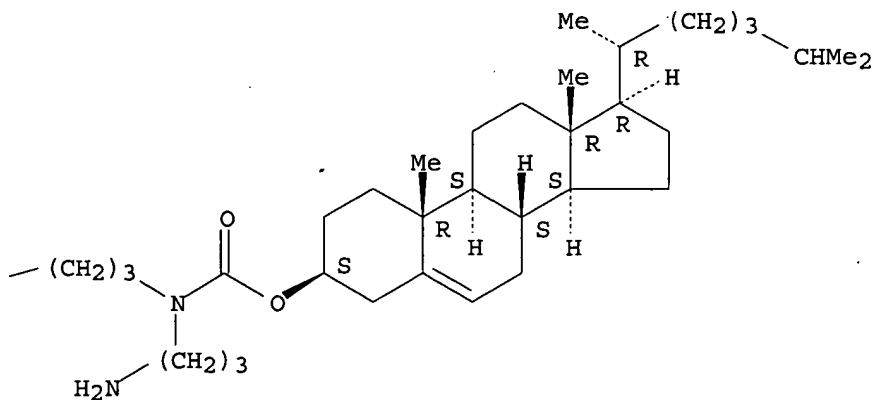
CN Cholest-5-en-3-ol (3 $\beta$ )-, (3-aminopropyl)[(4S)-4-[(3-aminopropyl)amino]-5-[(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenylamino]-5-oxopentyl]carbamate (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:635184 CAPLUS

DOCUMENT NUMBER: 130:151

TITLE: Structural requirements for arachidonylethanolamide interaction with CB1 and CB2 cannabinoid receptors: pharmacology of the carbonyl and ethanolamide groups  
AUTHOR(S): Berglund, B. A.; Boring, D. L.; Wilken, G. H.; Makriyannis, A.; Howlett, A. C.

CORPORATE SOURCE: Department of Pharmacological and Physiological Science, St Louis University School of Medicine, St Louis, MO, 63104, USA

SOURCE: Prostaglandins, Leukotrienes and Essential Fatty Acids  
(1998), 59(2), 111-118  
CODEN: PLEAEU; ISSN: 0952-3278  
PUBLISHER: Churchill Livingstone  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Analogs of arachidonylethanolamide (anandamide) were prepared to investigate the structural requirements for ligand binding to and activation of the CB1 and CB2 cannabinoid receptors. The importance of the presence and the placement of the carbonyl was examined with analogs lacking the carbonyl or with the carbonyl amide order reversed. The presence and location of the carbonyl is essential for high-affinity binding to both cannabinoid receptor subtypes, and for determination of signal transduction via G-proteins. Me groups were substituted on the 1'- and 2'-positions of arachidonylethanolamide and the significance of chirality was examined Stereochem. differences in the ethanolamide group influence the affinity for both cannabinoid receptor subtypes and the signal transduction capabilities of the methanandamide derivs.

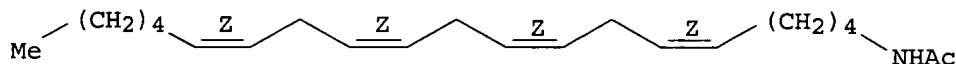
IT 215818-35-2P

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (structural requirements for arachidonylethanolamide interaction with CB1 and CB2 cannabinoid receptors in relation to pharmacol. of carbonyl and ethanolamide groups and activation of signal transduction)

RN 215818-35-2 CAPLUS

CN Acetamide, N-(5Z,8Z,11Z,14Z)-5,8,11,14-eicosatetraenyl- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1997:530855 CAPLUS

DOCUMENT NUMBER: 127:205874

TITLE: Synthesis and properties of novel lipopeptides and lipid mimetics

AUTHOR(S): Nicolaou, Anna; Kokotos, George; Constantinou-Kokotou, Violetta; Charitos, Christos; Noula, Caterina; Verger, Robert; Gibbons, William A.

CORPORATE SOURCE: University-Industry Centre for Pharmaceutical Research, The School of Pharmacy, University of London, London, WC1N 1AX, UK

SOURCE: Journal of Peptide Science (1997), 3(4), 291-298  
CODEN: JPSIEI; ISSN: 1075-2617

PUBLISHER: Wiley

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Lipid mimetics, synthetic mols. that resemble natural lipids either structurally or functionally, have been developed as potential medicinal substances. They have been successfully applied in the development of drug and peptide delivery systems and for the development of inhibitors or lipid metabolizing enzymes. Phospholipase A2 is considered to be involved as the rate-limiting step in the production of lipid mediators of inflammatory responses and, as such, it has been a target for drug design. A series of lipid mimetics including lipopeptides, amides and alcs. of lipidic  $\alpha$ -amino acids, have been tested by bulk and monolayer assay

techniques. The findings suggested the direct interaction of the tested compds. with porcine pancreatic phospholipase A2. The inactivation of the enzyme occurred in a competitive manner. The most active compound, 2-amino-N-hexadecyl-L-hexanamide, showed an apparent IC50 of 12  $\mu$ M and inhibitory power Z = 13 in the monolayer assay.

IT 194659-88-6P 194659-90-0P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation, properties, and phospholipase inhibitory activity of novel lipopeptides and lipid mimetics)

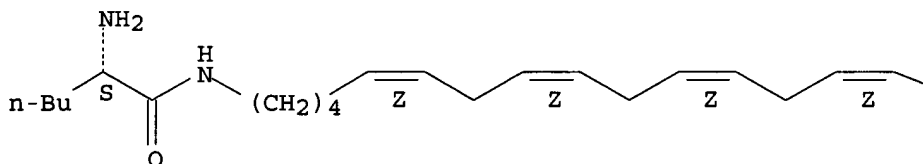
RN 194659-88-6 CAPLUS

CN Hexanamide, 2-amino-N-5,8,11,14-eicosatetraenyl-, monohydrochloride, [S-(all-Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

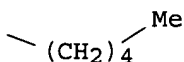
Double bond geometry as shown.

PAGE 1-A



● HCl

PAGE 1-B

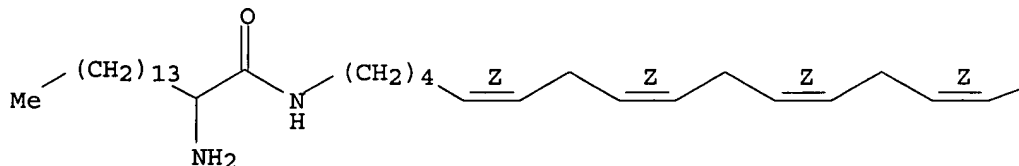


RN 194659-90-0 CAPLUS

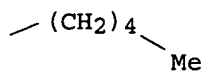
CN Hexadecanamide, 2-amino-N-5,8,11,14-eicosatetraenyl-, monohydrochloride, (all-Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



● HCl



IT 194659-87-5P 194659-89-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

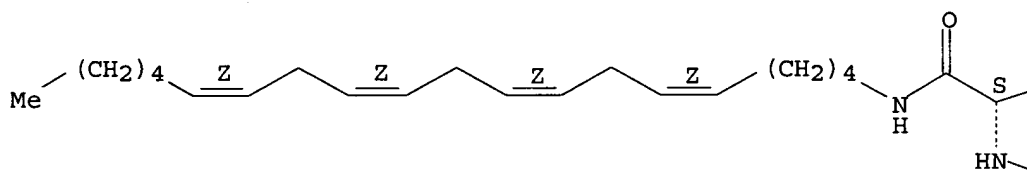
(preparation, properties, and phospholipase inhibitory activity of novel lipopeptides and lipid mimetics)

RN 194659-87-5 CAPLUS

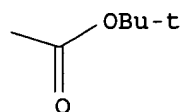
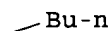
CN Carbamic acid, [1-[(5,8,11,14-eicosatetraenylamino)carbonyl]pentyl]-, 1,1-dimethylethyl ester, [S-(all-Z)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

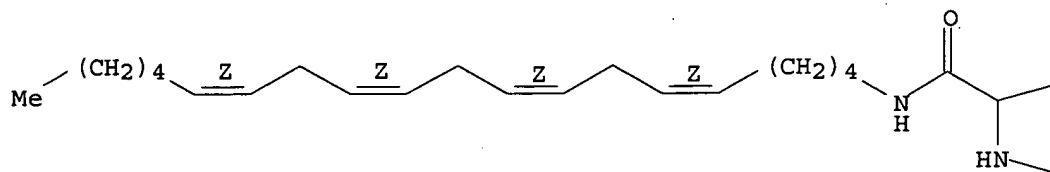


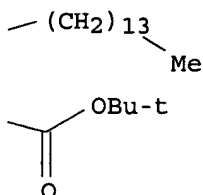
RN 194659-89-7 CAPLUS

CN Carbamic acid, [1-[(5,8,11,14-eicosatetraenylamino)carbonyl]pentadecyl]-, 1,1-dimethylethyl ester, (all-Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A





REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L33 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1987:598099 CAPLUS

DOCUMENT NUMBER: 107:198099

TITLE: Preparation of aminoethyl nicotinate derivatives as anticholesteremics and hypolipemics

INVENTOR(S): Takahashi, Keiko; Wakabayashi, Toshio

PATENT ASSIGNEE(S): Terumo Corp., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.

CODEN: JKXXAF

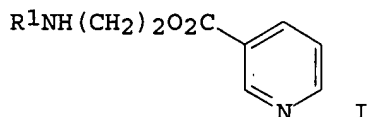
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 62106019	A2	19870516	JP 1985-245794	19851101
JP 02062531	B4	19901226		
EP 228314	A2	19870708	EP 1986-402442	19861031
EP 228314	A3	19900328		
R: BE, CH, DE, FR, GB, IT, LI, NL, SE				
US 4794115	A	19881227	US 1986-925239	19861031
PRIORITY APPLN. INFO.: GI			JP 1985-245794	A 19851101



AB The title compds. (I; R<sup>1</sup> = H, acyl moiety from higher trienoic or eicosapentaenoic fatty acids), useful as hypolipemics, were prepared A mixture of 1 g N-(9,12,15-octadecatrienoyl)-2-aminoethanol and 709 mg nicotinoyl chloride in CHCl<sub>3</sub> containing K<sub>2</sub>CO<sub>3</sub> was kept overnight to give 1.075 g I (R = 9,12,15-octadecatrienoyl) (II). The concentration of total cholesterol

in rats orally fed with 2.4 mM II/kg and a mixture of 10% cholesterol and 1% cholic acid in corn oil (10 mL/kg) for 7 days was 146.6 mg/dL, vs. 210 mg/dL in controls.

IT 111128-25-7

RL: RCT (Reactant); RACT (Reactant or reagent)  
(esterification of, in preparation of hypolipemic)

RN 111128-25-7 CAPLUS

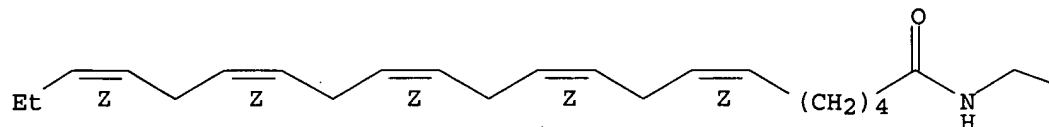
CN 6,9,12,15,18-Heneicosapentaenamide, N-(2-hydroxyethyl)-, (all-Z)- (9CI)

09/600,786

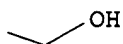
(CA INDEX NAME)

Double bond geometry as shown.

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PAGE 1-B



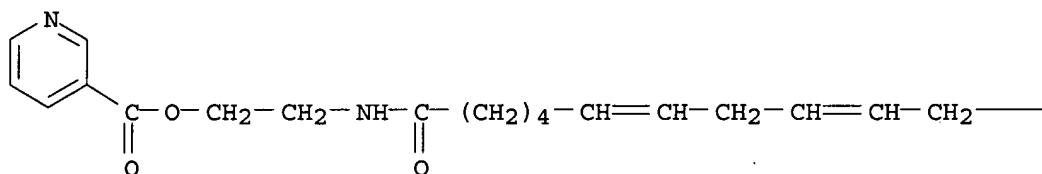
IT 111149-95-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as hypolipemic)

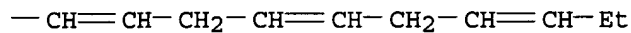
RN 111149-95-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 2-[(1-oxo-6,9,12,15,18-heneicosapentaenyl)amino]ethyl ester, (Z,Z,Z)- (9CI) (CA INDEX NAME)

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